Generisch. Virchow's Archiv, No. 94, 33.
Gluge. Abhandlungen zur Phys. und Path., 1841, 140.
Goldman. Beiträge zur klin. Chir., x.
Hansemann. Deut. med. Wochens., 1895, V. N., 133.
Herczel. Beiträge zur pathologischen Anatomie und zur allgemeinen Pathologie, 1890, No. 8, 38.
Hitchcock. Amer. Journ. Med. Sciences, April, 1862.
Hoisnard. Contribution à l'Étude de la neurofibromatose généralisée, Paris, 1898.
Iehl. De la dermatofibromatose pigmentaire géneralisée et de ses rapports avec la neurofibromatose pigmentaire généralisée, Paris, 1898.
Jopson. Arch. of Pediatrics, 1898, No. 15, 173.
Keen and Spiller. American Journal of the Medical Sciences, May, 1900.
Köbner. Virchow's Archiv, No, 93, 243.
Krause. Ueber maligne Neurome, Leipzig, 1887.
Kriege. Virchow's Archiv, No. 108, 466.
Küster. Berl. klin. Woch., 1884, No. 16, 243.
Lahman. Virchow's Archiv, No. 101, 263.
Landowski. Gaz. d. Hôp., 1896, 946.
Lannois et Variot. Revue d. Chir., 1883, No. 6.
Leredde. Ann. Dermat. et Syph., 1896, 3d S., No. 9, 46.
Marie et Bernard. Gaz. d. Hôp., 1896, 303.
Modrzejewski. Gaz. Hebdom., 1882, 508.
Neumann. Archiv für Dermat. und Syph., 1897, No. 39, 3.
Pean. Bull. d. l'Academie de Médecine, 1897, No. 37, 51.
Pomorski. Virchow's Archiv, 111.
Posadsky. Virchow's Archiv, No. 87, 382.
Prudden. Amer. Journ. Med. Sciences, 1880, 159.
Ramond. Bull. d. la Soc. Anat., 1896, 375.
Recklinghausen. Die multiplen Fibrome d. Haut, Berlin, 1882.
Schlange. Berl. klin. Woch., 1889, 122.
Schuster. Zeitsch. f. Heilk., 1886, Bd. vii.
Smith. Treatise on Neuroma. Reprinted by the New Sydenham Society, 1898.
Spillmann et Etienne, Gaz. Hebdom, 1898, 673.
Tailhefer. Le Progrès Medicale, 1897, 474.
Vejas. Aerztliches Intelligenzblatt, 1885, No. 26.
Verneuil et Depaul. Bull. d. la Soc. Anat., Paris, 1857.
Virchow. Die Krankh. Geschwülste, 111.
Von Arnozant. Journ. d. Méd. d. Bordeaux, September 20, 1885.
Von Büngner. Arch. f. klin. Chir., No. 55, 558.
Westphalen. Virchow's Archiv, No. 110, 29 and 114.
Winiwarter. Langenbeck's Archiv, Band xix.

THE RELATION OF CHOLELITHIASIS TO DISEASE OF THE PANCREAS AND TO FAT NECROSIS.

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Since the common bile-duct and the main duct of the pancreas unite in the diverticulum of Vater before reaching the lumen of the duodenum, changes occurring in one may produce pathological conditions in the other and consequent lesions of the liver or pancreas. The object of the present paper is to direct attention to the occurrence of pancreatic disease as a complication of gallstone colic, to the method of its occurrence, and to the nature of the lesions which ensue.

The association of the two conditions has been incidentally mentioned by a number of writers. In the several recently published monographs on diseases of the pancreas reference to it is made. Kôrte,[1] writing on the surgery of the pancreas, notes that diseases of the bile passages, especially cholelithiasis, are frequently associated with lesions of the pancreas, and thinks it is probable that inflammation can extend from the bile-duct to the gland. Oser[2] thinks that catarrhal inflammation may extend from the gall passages to the pancreatic duct, producing obstruction of the secretion and its consequences; the pancreatic duct may be occluded by a stone lodged in the common duct near its orifice. Lancereaux[3] mentions the possibility that a gallstone lodged in the common duct at the level of the diverticulum of Vater may occlude the pancreatic duct and produce conditions favorable to the penetration of micro-organisms into the pancreas. Ebstein[4] has recently reported a case of diabetes associated with attacks of abdominal pain. Seeking an explanation of the obscure symptoms, he discusses the interrelation of pancreatic and hepatic disease. He recalls the fact that the ductus communis choledochus and the duct of Wirsung enter the intestine side by side, so that a gallstone or a pancreatic calculus lodged near the orifice of either duct might occlude both.

Gallstones are not infrequently accompanied by inflammatory changes in various parts of the bile passages, and it is conceivable that secondary lesions of the pancreas may follow. The inflammatory process whose immediate cause is the presence and development of micro-organisms may extend along the common duct, to the diverticulum of Vater, be transmitted to the main pancreatic duct, and thence to the parenchyma of the organ. Biliary calculi may favor the occurrence of pancreatic lesions by another method. Lodged near the orifice of the common duct they may compress the neighboring duct of Wirsung and obstruct the outflow of the pancreatic juice. When the duct is wholly or partially occluded one may readily believe that, though the secretion of the gland cannot enter the intestine, micro-organisms may make their way from the duodenum into the dammed-back secretion, and, multiplying, produce inflammatory changes in the gland. The obstructed secretion, moreover, may be forced backward into the gland parenchyma, and, even though micro-organisms have not entered, may produce injurious effects upon the substance of the organ.

When the common bile-duct is occluded the secretion of the liver forced back upon the organ finds its way into the interstitial tissue, whence it is transmitted to more distant parts by way of the lymphatics and reaches the blood through the thoracic duct. The bile-pigments stain the tissues a conspicuous yellow color and indicate the presence of retained products of secretion. The pancreatic juice, on the contrary, containing no pigment, does not carry an index of its presence. When the pancreatic duct is occluded, do we find any evidence that the secretion has penetrated the surrounding tissue and there produced deleterious effects ?

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[1] Chirurg. Krankh. des Pankreas. Deutsche Chirurgie, Stuttgart, 1898.

[2] Die Erkrank. des Pankreas. Nothnagel's Spec. Path. u. Ther., Vienna, 1898, vol. xvii.

[3] Traite des malades des foie et des pancréas, Paris, 1899.

[4] Zeitsch. f. klin. Med., 1900, vol. xl. p. 181.

Disseminated fat necrosis was first accurately described by Balser in 1882. Not infrequently one finds studding the fat in the immediate neighborhood of the pancreas opaque, white areas, varying in size. Less frequently similar opaque foci are found in the omentum, mesentery, and subperitoneal fat of the abdominal walls ; rarely in the pericardial and subcutaneous fat. Microscopical examination shows that the fat cells in these areas are necrotic, and the micro-chemical studies of Langenhans[1] have demonstrated that the necrosis is associated with the splitting of the contained fat into its fatty acid and glycerin. The former, being insoluble, remains in the cell, and subsequently unites with calcium salts, while the soluble glycerin is absorbed and carried away. Various lesions of the pancreas have been found associated with fat necrosis, notably hemorrhagic and gangrenous pancreatitis, more rarely other changes. The investigations of Langenhans, Hildebrand and Dettmer, Milisch, Williams, Flexner, Katz and Winkler, and Opie have shown that the active factor in the production of necrosis of the fat cell and disintegration of the fat is the fat-splitting ferment of the pancreatic juice, which as the result of some lesion of the gland has made its way into the surrounding tissue and come in contact with the fat cells.

In a series of experiments recently reported[2] I have shown that ligation of both pancreatic ducts in the cat causes very wide-spread fat necrosis, involving almost the entire abdominal fat, at times the subcutaneous and pericardial fat, and reproduces the wide distribution occasionally observed in human beings and in animals. If the ducts are ligated and pilocarpin is subsequently administered to the animal in order to stimulate the secretion of the pancreas, the dissemination of the pancreatic secretion is much hastened and very wide-spread focal fat necrosis rapidly occurs. The experiments show that when the outflow of the pancreatic juice is obstructed the products of secretion, dammed back upon the gland, penetrate into the tissue surrounding it and produce alterations which serve as an indication of their presence. The pancreatic lesions which in human cases are associated with necrosis of fat are such as permit the penetration of the secretion into the tissue.

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[1] Virchow's Arch., 1890, vol. cxxii. p. 252.

[2] Contributions to the Science of Medicine. Dedicated to Wm. H. Welch, M. ., Baltimore, 1900, p. 859.

Fat necrosis may be regarded as an index of pancreatic disease, and is, therefore, an important factor in the study of lesions affecting the organ. The condition is a consequence of pancreatic lesions much as jaundice is a symptom of hepatic disease, and is not, therefore, an independent morbid entity.

In recording the experiments referred to above I have taken occasion to point out that obstruction of the pancreatic duct in human cases is not infrequently associated with disseminated fat necrosis. The condition occasionally follows occlusion of the duct by calculi or by carcinoma. Several cases are cited where gallstones were found lodged in the common bile-duct near its orifice in such a position that they might at the same time occlude the pancreatic duct.

The anatomical relations of the common bile-duct and the duct of Wirsung are well known. The common bile-duct descends toward the duodenum alongside the head of the pancreas, occasionally embedded in its substance, and comes in contact with the duct of Wirsung, beside which it lies for a short but variable distance before entering the wall of the intestine. The two ducts penetrate side by side the coats of the duodenum, and after passing obliquely a distance of about 2 cm. and causing a papilla-like elevation of the mucous membrane, unite to form a short cavity—the diverticulum of Vater. Near its termination, at a point where the two ducts are in contact, the common duct becomes constricted, and it is here that a foreign body passing downward tends to lodge.

Of considerable importance is the fact that occlusion of the main pancreatic duct does not necessarily cause complete obstruction to the outflow of the pancreatic secretion. The duct of Wirsung communicates within the gland with the accessory pancreatic duct or duct of Santorini, which opens into the duodenum at a point 2.5 to 3.5 cm. nearer the stomach. Schirmer[1] has studied the relation of the two ducts in a large number of human cases, and has found that it presents much variation. Among 104 bodies he found that in sixty-five instances the accessory pancreatic duct anastomosed with the larger within the organ and opened by a separate orifice into the duodenum. In one instance three ducts entered the duodenum. In four cases the common bile-duct alone opened into the diverticulum of Vater, while the single pancreatic duct entered the duodenum at a point corresponding to the usual site of the orifice of the accessory duct. In thirty-four instances the smaller duct did not anastomose with the larger or communicate with the duodenum. In the latter case alone would it be possible for a stone lodged in the diverticulum of Vater or in the common duct, where it comes in contact with the pancreatic duct, to obstruct completely the outflow of the pancreatic secretion. In only slightly more than one-third of the cases where gallstones lodge near the orifice of the common duct should one expect to find changes in the pancreas referable to duct obstruction.

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[1] Inaug. Diss., Basel, 1893.

Opportunity has recently been afforded for the study of a case in which lesions of the pancreas were associated with the impaction of a stone near the orifice of the common duct. In view of the obscurity in which the etiology of pancreatic lesions is still involved, it may be of interest to record the case and to compare it with others in which a similar etiological factor is more or less clearly demonstrable.

L. F., male, aged forty-seven years. The patient was admitted to the Johns Hopkins Hospital, service of Dr. Osler, complaining of abdominal pain and fever. His family history is unimportant. With the exception of rather frequent attacks of indigestion, characterized by pain after eating, distention, and rarely nausea and vomiting, he has enjoyed good health. He does not use alcohol in any form. Six months before his present illness he suffered from an attack of jaundice, lasting about three weeks, and accompanied by abdominal pain and some fever. His stools at this time were somewhat clay-colored. At the end of three weeks he felt perfectly well.

The present illness began eighteen days before admission to the hospital, when about 9 P.M. the patient was suddenly seized with violent nausea and vomiting, accompanied by intense cramp-like pain in the abdomen. The vomiting continued during the first night, and has since only occasionally recurred. The abdominal pain, which was not localized, remained severe during four or five days, and at times there were symptoms of collapse. The abdomen was distended and the bowels were constipated until the fifth day, when, with the aid of a purgative, movement occurred. The stool was normal in color. On the third day elevation of temperature to 101.5° F. was noted. About the seventh day tenderness and slight swelling were noticed in the right hypochondriac region. Since this time the patient has had an irregular temperature (100° to 103° F.), with several chills; the pulse, 100 to 120 a minute, has been at times dicrotic. Since the first few days the abdominal pain and tenderness have not been severe, but distention of the abdomen has gradually increased. Jaundice has not been noted

Physical Examination (note by Dr. Futcher). The patient is a large-framed man. The complexion is somewhat sallow and the conjunctivæ have a slightly yellow cast. The pulse is of fairly good volume, regular in force and rhythm. Examination of the heart and lungs is negative. On inspection of the abdomen the right costal groove is found to be partly obliterated. A distinct prominence occupies the right hypochondriac and right half of the epigastric region and extends into the upper half of the umbilical region. Its lower margin, which descends on inspiration, is felt in the median line at the level of the umbilicus; in the mammary line, 10.5 cm. below the costal margin. Its right border cannot be sharply defined. In the median line the fingers can be pressed in above it. Over the resistant mass there is dull tympany, continuous with the hepatic flatness. Leucocytes, 18,300. Urine, clear; specific gravity, 1017; acid. There is no reduction of Fehling's solution. A trace of albumin is present.

On the second day after admission a stool passed was of golden-yellow color. On the third day the leucocytes numbered 19,500, and the temperature varied from 99.2° to 101.8° F. During the night the patient was irrational at times. The temperature rose gradually, reaching a maximum of 104° F. A liquid stool of ochre-yellow color was passed. Urine: specific gravity, 1020; no reaction for sugar was obtained.

The diagnosis of suppurative pancreatitis was made by Dr. Bloodgood, and an operation for its relief was performed under cocaine anæsthesia. A linear longitudinal incision was made below the costal margin within the right mammillary line. After incising the great omentum between the stomach and transverse colon an abscess cavity was entered. Grumous, purulent fluid containing necrotic particles was evacuated. A rubber drainage-tube, packed about with gauze, was inserted into the wound. After operation the pulse remained weak, and death followed at the end of about four hours. The duration of the fatal illness was twenty-one days.

Autopsy. Performed three hours after death. The body is that of a large-framed, muscular man with abundant subcutaneous fat. *Peritoneal cavity:* The omentum, which contains a large quantity of fat, is adherent in the neighborhood of the operation wound to the anterior abdominal wall by light, fibrinous adhesions. Its surface is thickly studded with conspicuous opaque, white areas, varying in size and shape, but usually round and about 3 mm. in diameter, extending about 1.5 mm. below the surface. On section similar foci are found embedded in the fat. Opaque, white areas are present in the fat of the mesentery, where they are most abundant near its intestinal margin, in the subperitoneal fat of the anterior abdominal wall, over the bladder, over the kidneys, and about the colon. *Abscess cavity:* The drainage-tube inserted into the abdominal wound passes through a small, incised opening in the great omentum and enters an immense abscess cavity which occupies approximately the site of the lesser peritoneal cavity. The foramen of Winslow is closed. The stomach is pushed upward and forward, and its anterior surface is adherent to the lower surface of the liver to the left of the gall-bladder. The spleen, partially surrounded by fat containing many opaque, white areas, is bound by fibrous adhesions to the diaphragm. The walls of the cavity are very irregular and ragged, and have a necrotic appearance, in general opaque and gray, occasionally black. This blackish-gray appearance extends only a short distance below the surface, and where the wall is formed by fat give place to numerous foci of opaque, white color. The retroperitoneal fat in front of the left kidney and psoas muscle has been eroded, and an extension of the cavity passes behind the jejunum near its junction with the duodenum. To the left of the descending portion of the duodenum, occupying the position of the pancreas and projecting forward into the abscess cavity, is a great mass of black material, necrotic in appearance, extending to the left as far as the spleen. This material is reddish-black on section, somewhat spongy in texture, soft, dry, and friable. The cavity contains a large quantity—at least 500 c.c. of fluid reddish-gray material, containing fat droplets and black, necrotic particles.

Liver. The organ is flaccid in consistence; the cut surface has a brownish-red color; lobulation is well marked. The bile-ducts are slightly dilated, and contain thin, yellow bile. The gall-bladder is bound by numerous adhesions to the duodenum and stomach. Its walls are thickened, and it is much distended, containing viscid, yellow bile and a large number—over one hundred—of brown, faceted calculi, varying in diameter from 0.5 to 1 cm. The hepatic, cystic, and common ducts are much dilated. On opening the duodenum a stone is felt below the mucous membrane, situated in the common bile-duct, about 1.5 cm. from the orifice of the diverticulum of Vater. It is 7 mm. in diameter and resembles those present in the gall-bladder. *Pancreas:* The pancreatic duct unites with the common bile-duct at a point 7 mm. from the duodenal orifice. For a distance of 1.5 cm. the two ducts are separated by a thin septum only, and in contact with this septum is lodged the gallstone previously mentioned. The pancreatic duct is not distended. The pancreas occupies the posterior wall of the lesser peritoneal abscess cavity, and is covered by the mass of reddish-black, friable material, changed coagulated blood, above described. The organ is of large size, and the glandular tissue is in great part firm, yellowish-white, and well preserved. The interstitial tissue has a dull reddish, in places hemorrhagic, appearance, and contains conspicuous opaque, yellow areas of irregular shape. Where the anterior surface of the head and body is in contact with the overlying material there is a superficial zone of soft, grayish, necrotic appearance.

The other organs—heart, lungs, spleen, stomach, intestines, and kidneys—present no noteworthy alteration.

Histological Examination. The foci of fat necrosis consist of a central mass of necrotic material, in which the outlines of the fat cells are in most places preserved, though the nuclei have disappeared, and a peripheral zone of cell proliferation. The latter consists in part of large, round cells, with round or slightly irregular, deeply staining nucleus and granular or vacuolated cell body. Multinuclear cells of similar appearance are present. About neighboring bloodvessels lymphoid and plasma cells are accumulated in moderate number, together with an occasional polynuclear leucocyte.

The interstitial tissue of the pancreas is much increased, wide bands of fibrous tissue containing in places lymphoid and plasma cells, separate groups of lobules. Numerous irregularly shaped cells filled with brownish-yellow pigment granules, which give the Prussian-blue reaction for iron, afford evidence of former hemorrhage. In a few places well-preserved red corpuscles are diffusely scattered in the tissue. Foci of necrotic fat are present. Many acini are widely dilated; their cells are flat and the lumen is much distended, containing products of secretion and occasionally one or more polynuclear leucocytes. In an area corresponding to the zone of necrotic appearance before mentioned, nuclei no longer stain, and the architecture of the glandular tissue is only obscurely distinguishable. A thick band of newly formed fibrous tissue containing an occasional acinus or duct separates the necrotic parenchyma from that which is still intact. The mass covering the pancreas is found to consist of altered blood; upon and immediately below its surface are numerous polynuclear leucocytes.

Sections of the diaphragm, stomach, and liver where they form part of the abscess wall show a zone of newly formed fibrous tissue, upon the surface of which are necrotic material and polynuclear leucocytes in great number.

Bacteriological Examination. Cultures from the blood contained in the heart, from the lung, and from the liver, studied by Mr. V. H. Bassett, were found to contain the bacillus coli communis. A plate culture from the material covering the pancreas, and forming part of the abscess wall, contained the B. coli communis, the B. lactis aërogenes, and the B. proteus vulgaris.

Anatomical Diagnosis. Cholelithiasis; calculus lodged in the common duct near its orifice; slight jaundice. Old hemorrhage within and about the pancreas; localized necrosis of pancreas; chronic interstitial pancreatitis; necrosis of fat of pancreas, greater and lesser omentum, mesentery, and subperitoneal tissue of abdominal wall. Peripancreatic abscess limited by lesser peritoneal cavity. Laparotomy wound.

Symptoms occurring six months before the fatal illness indicated the passage of a calculus along the common duct, and this diagnosis was confirmed at autopsy by the presence of numerous calculi in the gall-bladder. The second attack began suddenly, three weeks before death, with severe nausea and vomiting, accompanied by intense, cramp-like pain in the abdomen. Tenderness was present in the right hypochondriac region, and on admission to the hospital the patient was slightly jaundiced. A mass was felt in the epigastrium; there was irregular fever and a leucocytosis of 18,000 to 19,000. The diagnosis of acute suppurative pancreatitis was made.

The autopsy disclosed a small gallstone lodged in the common bile-duct, a short distance from its orifice, in such a position that it might readily have compressed and occluded the duct of Wirsung, here separated from the bile-duct by a thin, almost membranous septum. The lesser peritoneal cavity was the site of a large abscess, whose walls were formed in large part by necrotic fat; the subperitoneal tissue was studded with conspicuous opaque, white foci of fat necrosis. The pancreas was in great part well preserved, but its interstitial tissue was increased and gave evidence of having been the seat of hemorrhage. The anterior surface of the pancreas was covered by a considerable quantity of old, clotted blood, having the dark appearance of gangrenous tissue and forming the tumor mass, which was palpable during life. A superficial zone of gland parenchyma in contact with this material was necrotic. There was evidence of duct obstruction; though the larger ducts were not dilated, many alveoli were dilated, and there was an increase of interstitial tissue.

Since jaundice was slight and the pancreatic duct was not dilated, it is probable that the calculus produced only temporary obstruction of the two ducts. Nevertheless, one may fairly assume that the primary cause of the lesions in and about the pancreas was an interference with the outflow of the pancreatic secretion. In support of this conclusion I have been able to collect from the literature a number of cases in which, associated with a lesion of the pancreas or with necrosis of the surrounding fat, usually with both conditions, a gallstone was found lodged in the common duct near its orifice, where it could compress the pancreatic duct, or, perhaps, free in the duodenum, the common duct being dilated (Cases I. and V.). In the latter case there could be little doubt that it has shortly before occupied the first-named position.

CASE I.[1]—Male, aged sixty years. During sixteen months the individual had suffered attacks of pain, followed by jaundice. He was suddenly attacked with severe pain in the left hypochondriac and epigastric regions. Collapse preceded death, which followed within thirty-four hours after the onset of symptoms. The thickened gall-bladder contained over a hundred calculi. The common bile-duct was dilated to the size of the little finger, and in the duodenum was a calculus the size of a hazel-nut. The pancreas was large, grayish-pink or reddish-gray, mottled with reddish-brown. Surrounding fat was moderately infiltrated with blood, and contained foci of necrosis.

CASE II.[2]—Male, aged forty-nine years. For several months the patient had suffered with pain in the epigastrium, at times in the right hypochondrium. His stools were occasionally clay-colored, and once he was jaundiced. About sixteen hours before death he was suddenly attacked with vomiting and severe epigastric pain, followed by collapse. "The gall-bladder contained one small concretion of inspissated bile; two others were lodged in the duodenal extremity of the common duct." The body and tail of the pancreas were enlarged and infiltrated with blood, exuding a chocolate-colored fluid. In the neighborhood of the gland were foci of fat necrosis.

CASE III.[3]—No clinical history is given. In the common duct close to its orifice was a gallstone; others are present in the duct behind it and in the gall-bladder. The body and tail of the pancreas were beset with green and yellow points, the tail being almost completely necrotic. Old and recent hemorrhages occur. Microscopical examination demonstrated the presence of suppurative inflammation, having its origin apparently in the ducts.

CASE IV.[4]—Female, aged fifty-eight years. For fifteen years she had suffered with severe attacks of indigestion, on one occasion followed by jaundice; pain in the right hypochondriac region occurred during the later attacks. Four days before death she was seized with pain in the right hypochondrium, accompanied by vomiting, chill, and fever, and followed by jaundice. A small gallstone was found at the outlet of the common duct; others were present in the gall-bladder. The pancreas was enlarged, surrounded and infiltrated with blood. Numerous foci of fat necrosis were seen in its neighborhood.

CASE V.[5]—Female, aged forty-eight years. The patient stated that she had suffered for years with stomach and liver trouble. Illness began five days before death, with vomiting, constipation, and abdominal distention; jaundice followed. The thickened gall-bladder contained three large concretions. In the duodenum was a stone the size of a cherry, and the papilla biliaria was gaping. In the interstitial tissue of the pancreas, which was fairly firm, were foci of fat necrosis; otherwise the organ appeared to be normal. Areas of necrosis were present in the fat of the greater and lesser omentum and of the appendices exploica.

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[1] Thayer. Boston Med. and Surg. Journ., 1889, vol. cxxi. p. 506.

[2] Day. Ibid., 1892, vol. cxxvii. p. 569.

[3] Dieckhoff. Festschr. f. Prof. Thierfelder. Leipzig, 1895.

[4] Cutler. Boston Med. and Surg. Journ., 1895, vol. cxxxii. p. 354.

[5] Fraenkel. Münchener med. Wochensch., 1896, vol. xliii. pp. 814, 844.

CASE VI.[1]—Female, aged thirty-eight years. The individual was suddenly seized forty-two hours before death with vomiting and pain in the upper part of the abdomen, followed by symptoms of collapse. A gallstone, about the size of a pea, was found projecting from the orifice of the common duct into the duodenum. Other calculi were found in the gall-bladder and common bile-duct. The pancreas was enlarged, and its appearance of intense injection was evidently due to inflammatory change. Slight peritonitis was present.

CASE VII.[2]—Male, aged forty-one years. The patient was suddenly attacked with vomiting and severe abdominal pain. Collapse preceded death, which occurred at the end of forty-four hours. A small, cubical gallstone projected from the end of the common duct into the duodenum; similar concretions were found in the gall-bladder. The pancreas was greatly enlarged, weighing 525 grammes, and mottled with areas of reddish-brown color, due to hemorrhagic infiltration of its interstitial tissue. The organ was surrounded by semifluid, clotted blood, of dark-brown color. The intima of the splenic artery was of a dirty-blue color, and apparently necrotic about 2 cm. from the aorta; the writer regards this vessel as the source of the hemorrhage, although it is not stated that rupture had occurred.

In the preceding eight cases a calculus had lodged in the common bile-duct near its orifice, or, having been expelled from this position shortly before death, lay in the duodenum, leaving the common duct dilated. Necrosis of the fat in or about the pancreas occurred in seven of these eight cases; in the report of the eighth case (No. 6), briefly described several years after its occurrence, no reference is made to this change. Even in the absence of gross lesions of the gland, as in Case No. 5, the occurrence of fat necrosis is not surprising, since the experiments previously mentioned have shown that simple duct ligation is followed by this change. In the remaining cases macroscopical alterations were observable.

In five instances recent hemorrhages had occurred into the organ, but, microscopical examination being omitted, it is difficult to determine whether these cases should be classified as examples of simple hemorrhage or of hemorrhagic pancreatitis. In the case which I have recorded there was evidence of past hemorrhage into and about the pancreas, accompanied by necrosis of a small portion of the organ. The remainder of the gland was the seat of chronic interstitial change, and apparently, as the result of invasion of micro-organisms into the hemorrhagic and necrotic tissue, an abscess, limited by the lesser peritoneal cavity, had formed about the organ. In Case No. 3 there were old and recent hemorrhages into the pancreas, which had undergone suppurative inflammation and necrosis.

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[1] Kennan. Brit. Med. Journ., 1896, vol ii. p. 1442.

[2] Simpson. Edinburgh Med. Journ., 1897, vol. ii. p. 245.

Of special interest are the four cases (Nos. 1, 2, 6, and 7) in which death occurred within thirty-three, sixteen, forty-two, and forty-four hours after the onset of sudden vomiting, pain in the upper abdomen, and collapse. The brief duration of symptoms indicates that the calculus found at autopsy had been lodged a short time only in the common duct. Nevertheless, extensive lesion of the pancreas, hemorrhagic in character, had resulted. In the study of reported cases it is often difficult to distinguish between hemorrhage into the pancreas and hemorrhagic pancreatitis. Indeed, the relation which the two conditions bear to one another is not clear. Various writers discuss the possibility of hemorrhage without pre-existing inflammation. Is hemorrhage the result of preceding inflammatory changes, or is inflammation a consequence of the secondary infection of an organ already the seat of hemorrhage? Histological and experimental studies have failed to explain the etiology of the two conditions.

Ligation of the pancreatic ducts in animals does not cause hemorrhage or hemorrhagic inflammation. By injecting the bacillus pyocyaneus and the bacillus diphtheriæ into the pancreatic duct, Flexner[1] obtained intensely hemorrhagic inflammation of the gland in several instances within forty-eight hours. It is conceivable that partial occlusion of the pancreatic duct associated with the invasion of the retained secretion by micro-organisms from the duodenum might cause a similar hemorrhagic lesion.

Should a calculus lodge so firmly in the common bile-duct as to cause obstruction to the outflow of the pancreatic secretion, one would also expect occlusion of the bile-duct and consequent jaundice. Where death rapidly follows, as in Cases Nos. 1, 2, 6, and 7, its absence is not surprising. Jaundice was present in Cases Nos. 4 and 5; in the case which I have recorded it was present in slight degree. The occurrence of advanced lesions in cases which have died within forty-eight hours after the onset of symptoms shows that a profound alteration might be produced by the transient impaction of a calculus, perhaps of insufficient duration to produce jaundice.

The preceding cases include only those in which there is positive evidence that a stone passing along the common bile-duct had become impacted in such position that occlusion of the pancreatic duct might ensue. A calculus might be temporarily so located and cause severe injury to the gland, but finally, being expelled, give no evidence of its former impaction. I have collected from the literature a number of cases in which pancreatic lesions and fat necrosis were associated with cholelithiasis. Gallstones were found in the gall-bladder or gall-ducts, but at autopsy there was not convincing evidence, as in the previously cited cases, that a stone in the common duct had occluded the pancreatic duct. In one of these cases (No. 9) a calculus had found its way into the pancreatic duct and caused suppurative inflammation.

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[1] Contributions to the Science of Medicine. Dedicated to Wm. H. Welch, M.D., Baltimore, 1900, p. 743.

No.	Author.	Duration.	Pancreas.	Fat necrosis.
1	Thayer[1]	34 hours	Hemorrhagic	Present.
2	Day[2]	16 hours	Hemorrhagic	"
3	Dieckhoff[8]	....	Hemorrhagic, purulent, and gangrenous	"
4	Cutler[4]	4 days	Hemorrhagic	"
5	Fraenkel[5]	5 days	....	"
6	Kennan[6]	42 hours	Hemorrhagic.	
7	Simpson[7]	44 hours	Hemorrhagic	Present.
8	Opie[8]	21 days	Hemorrhagic and gangrenous	"
9	Dieckhoff[3]	2 days	Purulent	"
10	Rolleston[9]	2 days	Hemorrhagic	"
11	Paul[10]	30 hours	Hemorrhagic.	
12	J. A. Smith[11]	24 hours	Hemorrhagic.	
13	Chiari[12]	7 days	Gangrenous	Present.
14	Chiari[13]	3 weeks	Gangrenous	"
15	Mader[14]	13 days	Gangrenous	"
16	Fitz[15]	10 days	Gangrenous	"
17	Simon and Stanley[16]	3 days	Purulent	"
18	Morian[17]	27 days	Hemorrhagic and gangrenous	"
19	Habersohn[18]	4 months	Gangrenous.	
20	Chiari[13]	2 months	Gangrenous.	
21	König[19]	32 days	Gangrenous	Present.
22	Rolleston[9]	2½ months.	Purulent	"
23	Hawkins[20]	4 days	....	"
24	Körte[21]	4 months	Gangrenous.	
25	Körte[21]	1 month	Hemorrhagic and gangrenous	Present.
26	Stockton & Williams[22]	3 weeks	....	"
27	Fraenkel[23]	....	Gangrenous	"
28	Fraenkel[23]	5 days	Hemorrhagic and gangrenous	"
29	Flexner[24]	....	....	"
30	Ehrich[25]	1 month	Gangrenous	"
31	Scott[26]	15 days	Gangrenous	"
32	Grawitz[27]	32 days	Gangrenous	"

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[1] Boston Medical and Surgical Journal, 1889, vol. cxxi. p. 506.

[2] Ibid., 1892, vol. cxxvii. p. 569.

[3] Festschrift f. Prof. Thierfelder, Leipzig, 1895.

[4] Boston Medical and Surgical Journal, 1895, vol. cxxxii. p. 354.

[5] Münch. med. Wochensch., 1896, vol. xliii. p. 813.

[6] British Medical Journal, 1896, vol. ii. p. 1442.

[7] Edinburgh Medical Journal, 1897, vol. ii. p. 245.

[8] See above.

[9] Transactions Pathological Society, London, 1893, vol. xliv. p. 71.

[10] Boston Medical and Surgical Journal, 1894, vol. cxxx. p. 8.

[11] British Medical Journal, 1897, vol. ii. p. 468.

[12] Wiener med. Wochensch., 1876, vol. xxvi. p. 291.

[13] Ibid., 1880, vol. xxx. pp. 139, 164.

[14] Bericht d. k. k. Krankenanstatt Rudolfs-Stiftung, 1884; 1885, pp. 371, 435.

[15] Medical Record, 1889, vol. xxxv. pp. 197, 225, 253.

[16] Lancet, 1897, vol. i. p. 1325.

[17] Münch. med. Wochensch., 1899, vol. lxvi. p. 348.

[18] Diseases of the Abdomen, 1878, 3d ed., p. 338.

[19] Inaug. Diss., Kiel, 1889.

[20] Transactions Pathological Society, London, 1893, vol. xliv. p. 78.

[21] Arch. f. klin. Chir., 1894, vol. xlviii. p. 721.

[22] AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1895, n. s., vol. cx. p. 251.

[23] Münch. med. Wochensch., 1896, vol. xliii. pp. 813, 844.

[24] Journal of Experimental Medicine, 1897, vol. ii. p. 413.

[25] Beiträge z. klin. Chir., 1898, vol. xx. p. 316.

[26] AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1899, n. s., vol. cxviii. p. 414.

[27] Münch. med. Wochensch., 1899, xlvii. p. 813.

The first eight cases of the table are those already cited.

A hemorrhagic lesion of the pancreas, hemorrhage or hemorrhagic pancreatitis, was present in Cases Nos. 10, 11, and 12. Gallstones were found in the gall-bladder or in the bile passages, but there is no record that a calculus was located near the orifice of the common duct. Jaundice was absent, and the autopsy gave no positive evidence that a stone had recently passed into the duodenum. Death followed within forty-eight hours the onset of symptoms, abdominal pain, vomiting, and collapse. The clinical and pathological picture agrees with that of the preceding cases of rapidly fatal hemorrhagic lesion (Nos. 1, 2, 6, and 7). One factor alone is absent: the offending calculus has apparently been passed into the intestine and lost.

When, it may be, with a history of previous gallstone colic, the fatal attack is accompanied by evidence of the passage of a calculus along the common duct, notably pain and jaundice, and calculi are found in the bile passages after death, though none are found near the orifice of the common duct, one is justified, in view of the more conclusive cases mentioned (Nos. 1 to 8), in assuming that the pancreatic lesion was caused by a calculus temporarily occluding both ducts, but finally expelled and evacuated. The reports of cases Nos. 13 to 18 show that they fulfil these conditions; in all of them well-marked jaundice was present.

In the remaining cases (Nos. 19 to 32), although death did not follow shortly after the onset of symptoms, jaundice was not present, and the clinical history gives insufficient evidence that a stone had passed along the common duct. It is not improbable that in some of these cases the association of pancreatic lesion and cholelithiasis was accidental. On the other hand, it is well known that jaundice does not always follow the passage of a calculus through the common duct. Cases cited above have shown that extensive hemorrhagic lesion of the pancreas may be caused by a stone which has only a short time occluded the pancreatic duct. Where death has not followed rapidly the onset of symptoms, gangrenous pancreatitis, often with evidence of old hemorrhage, is observed.

The cases of acute pancreatic lesion recorded in the literature are not numerous; the relatively large number which have been found associated with cholelithiasis indicates an intimate relation between the two processes, and in view of the facts above noted it is fair to assume that with few exceptions the pancreatic lesion in the collected cases was caused by the presence of gallstones. They number thirty-two.

In twenty-six cases fat necrosis was present. In three of the six cases where it was absent (Nos. 6, 11, and 12) death occurred very soon after the onset of symptoms. In four instances (Nos. 5, 23, 26, and 29) fat necrosis was present, though no gross lesion of the pancreas was noted.

In seven cases (Nos. 1, 2, 6, 7, 10, 11, and 12) death followed the onset of symptoms—abdominal pain, vomiting, and collapse—within forty-eight hours, and at autopsy hemorrhagic infiltration of the pancreas was present. In an eighth case (No 4) death followed in four days. In these cases, as mentioned above, it is not possible to determine whether the gland was the seat of simple hemorrhage or of hemorrhagic pancreatitis. It is probable that the lesion is that usually described as hemorrhagic pancreatitis; here the organ is infiltrated with blood, and there is necrosis of greater or less extent combined with inflammatory changes.

In the great majority of the cases where the fatal illness was of longer duration the pancreas presented the lesion usually described as gangrenous pancreatitis. This condition was present in seventeen cases. The organ is dry, friable, blackish, and necrotic in appearance. Old, changed blood frequently gives evidence of former hemorrhage, and there can be little doubt that this so-called gangrenous pancreatitis represents a late stage of the hemorrhagic lesion. In a large proportion of such cases infection of the injured organ and of the necrotic fat occurs, presumably from the duodenum, and a peripancreatic abscess results, usually limited by the wall of the lesser peritoneal cavity whose fat has become in large part necrotic.

In three cases (Nos. 9, 17, and 22) the pancreas was the seat of suppurative inflammation, apparently without hemorrhage or necrosis. In one of them (No. 9) a gallstone had found its way into the pancreatic duct.

The cases previously cited include only acute lesions of the pancreas. Accompanying long-continued occlusion of the pancreatic ducts one usually observes chronic changes in the gland, chronic interstitial inflammation, dilatation of the ducts, and occasionally the formation of retention cysts. Phulpin[1] has recorded a case in which a stone lodged for a long time near the junction of the common bile-duct and duct of Wirsung occluded both:

> A woman, aged seventy-four years, had suffered with jaundice for a year and a half. At autopsy the gall-bladder was found to contain numerous faceted calculi the size of pease. The common bile-duct was so dilated that its diameter almost equalled that of the small intestine. At a point about 2 cm. from its orifice it assumed its usual size, and here was lodged a calculus similar to those found in the gall-gladder. Irregularly scattered in the body and tail of the pancreas were a score of cysts the size of hazel-nuts. The duct of Wirsung was dilated to the size of the index finger. Passing toward the duodenum the dilatation ceased at a point where the pancreatic duct comes in contact with the common bile-duct before traversing with it the wall of the duodenum and opposite the calculus lodged in the common duct. No accessory pancreatic duct could be found.

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[1] Phulpin. Bull. Soc. Anat. d. Paris, 1892, vol. lxvii. 5me. S. 6.

In two cases recently reported by Mayo Robson,[1] where operation was performed for removal of gallstones from the common duct, the head of the pancreas was found so indurated that a diagnosis of malignant growth was made. In one of these cases autopsy demonstrated the presence of chronic interstitial pancreatitis. Since in the second case the subsequent history disproved the diagnosis of malignant disease, Robson thinks that here also chronic pancreatitis was present.

In the following case chronic interstitial pancreatitis and fat necrosis was associated with cholelithiasis:

Anatomical Diagnosis. A. G., female, aged fifty years. Cholelithiasis; calculi in gall-bladder, cystic, hepatic, and common bile-ducts. Focal necrosis of liver and acute suppurative inflammation of bile-ducts. Adenocarcinoma of the gall-bladder; metastases in liver. Jaundice. Chronic interstitial pancreatitis. Peripancreatic fat necrosis. Hemorrhage into the gastro-intestinal canal; submucous ecchymosis. Acute spleen tumor; ascites.

Synopsis of Autopsy Protocol. The body is that of a large, well-nourished woman, deeply jaundiced.

The liver, weighing 2250 grammes, has a dark, greenish-yellow color; the bile-ducts are dilated. On the upper surface of the left lobe are several bleb-like projections, the largest 8 mm. across, containing yellow, pus-like fluid. The gall-bladder notch is deep, and the surface of the liver in its neighborhood is much puckered. On freeing adhesions with the duodenum the gall-bladder is found to be firmly contracted over a number of faceted concretions of an average diameter of about 12 mm. The inner surface of the cavity is rough and irregular in shape; its wall where it comes in contact with the under surface of the liver has an average thickness of 6 mm., and is formed by dense, gray-white tissue, which sends short projections upward into the liver substance. Sparsely scattered throughout the liver are small nodules, usually about 5 mm. in diameter, composed of similar tissue. The cavity of the gall-bladder communicates with a second cavity of considerable size, representing apparently the junction of the hepatic, cystic, and common bile-ducts, and containing two faceted stones, each about 1 cm. in diameter. Otherwise the common duct is not markedly dilated, having a circumference of 4 mm., but its walls are somewhat thickened and fibrous.

The pancreas is very firm in consistence, and is infiltrated with and embedded in fat. In the body of the organ are several conspicuous areas of irregular shape, 2 or 3 mm. across, composed of opaque, yellowish-white material. Similar foci of smaller size are sparsely scattered in the interstitial fat throughout the organ. The lumen of the duct of Wirsung is conspicuous, but not markedly dilated.

Histological Examination. Foci of necrosis and of acute inflammation are present throughout the liver. The tissue replacing the gall-bladder where it comes in contact with the liver and the nodules throughout the organ have the structure of adenocarcinoma.

The interstitial tissue of the pancreas is increased throughout the gland, most markedly in the tail, and the normal lobulation of the gland is much more distinct than usual. Fat is very abundant, and contains foci of necrosis surrounded by cells of lymphoid and epithelioid type in moderate number, together with many polynuclear leucocytes. The medium-sized ducts are much dilated, their cells are flattened, and they contain products of secretion, desquamated cells, and occasionally a few polynuclear leucocytes. In general the acini are normal in appearance, but many are considerably dilated and contain an occasional polynuclear leucocyte.

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[1] Lancet, 1900, vol. ii. p. 235.

In the preceding case the changes in the pancreas are those which usually follow duct obstruction; the ducts throughout the gland are dilated, the interstitial tissue between groups of lobules is much increased, and contains foci of fat necrosis. The common bile-duct, which is the seat of chronic inflammation, contains numerous calculi, and one may readily believe that the pancreas has suffered during the expulsion of gallstones.

The preceding study has shown that where anatomical conditions are favorable disease of the pancreas may occur as a complication of cholelithiasis when a calculus passes along the common bile-duct. The lodgement of a stone near the orifice of the bile-duct, where it may at the same time compress and occlude the duct of Wirsung, is not uncommonly a cause of pancreatic lesions and disseminated fat necrosis. Should a calculus become impacted in this position the preceding cases have shown that one of several conditions may result:

1. An individual, usually in fairly good health, with perhaps a history of previous gallstone colic, is suddenly attacked with pain in the epigastric region, accompanied by vomiting and followed by collapse. Death follows usually within forty-eight hours, and at autopsy gallstones are found in the bile passages, while that one which caused the fatal attack may be still lodged in the common duct near its orifice. The pancreas is enlarged, infiltrated with blood, and hemorrhage may have occurred into the surrounding tissue. Foci of fat necrosis are usually present.

2. A fatal termination may not follow rapidly the symptoms mentioned. Pain in the epigastrium persists, jaundice may be present, and a tumor mass above the umbilicus may indicate a probable lesion of the pancreas. At the end of one or more weeks or months death occurs, often with symptoms indicating the presence of suppurative inflammation, presumably in the neighborhood of the gland. At autopsy the diagnosis of cholelithiasis is confirmed by the presence of gallstones in the gall-bladder or in the bile-ducts, and occasionally the offending calculus is still lodged near the junction of the common bile-duct and the duct of Wirsung. The pancreas is dry, black, and necrotic, and evidence of previous hemorrhage may be present. Secondary infection has occurred and the pancreas lies in an abscess cavity formed by the bursa omentalis. In the wall, and often widely disseminated in the

abdominal fat, are foci of necrosis. Since the individual has survived the primary lesion opportunity has been given for the development of secondary changes in the injured pancreas and neighboring fat.

3. In certain instances long-continued or repeated obstruction of the pancreatic duct by gallstones does not cause the acute lesions described, but produces chronic inflammatory changes.

A REPORT OF A CASE OF TYPHOID PLEURISY.

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Pleurisy is not a common complication of typhoid fever; when present it is ordinarily secondary to pneumonia, to an infarction, or to gangrene. Primary pleurisy is regarded as very rare. Bacteriological study usually shows the presence of the more common members of the pyogenic group of micro-organisms. However, a few isolated reports in literature demonstrate the etiological relationship of the typhoid bacillus to certain cases. Thus fifteen years ago Rendu and de Gennes[1] claimed to have isolated the bacillus typhosus from the pus of an empyema. Two years later A. Fraenkel[2] reported a similar case. These reports were followed by others. In 1889, Valentini[3] isolated the typhoid organism from a purulent pleural exudate; then Mya and Belfanti,[4] in 1890, from a pleural abscess; and Weintraud[5] still later from a case of purulent pleurisy. More recently other examples have been published by Dineur,[6] Gerhardt,[7] and Souques, Lesnè and Ravaut.[8]

The history of the case reported by us is as follows:

The patient, a physician, aged fifty-seven years, was seen by Dr. Gordinier in consultation at Schaghticoke, N. Y., July 14, 1899. He presented the following history: In 1858, was ill several weeks with inflammatory rheumatism. In 1862, had, while in Virginia, typhus

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[1] Rendu and de Gennes. La France Médicale, 1885, vol. ii. p. 1821.
[2] A Fraenkel. Verhandlung sechste Kongress f. inner. Med., 1887, p. 179.
[3] Valentini. Berl. klin. Wochenschrift, 1889, p. 368.
[4] Mya and Belfanti Giornale d. Acad. di Med. di Turino, January, 1890.
[5] Weintraud. Berlin. klinische Wochenschrift, 1893, p. 345.
[6] Dineur. Bull. de l'Acad. Royale de Med. de Belgique, 1897.
[7] Gerhardt. Mittheilungen a. d. Grenzgebieten der Med. u. Chir., Bd. 1900, Heft 1.
[8] Souques, Lesnè and Ravaut. Bull. et Mém. de la Soc. Med. de Paris, January 25, 1900.